In the Claims

Please amend the claims presented during the international phase as follows. Applicant presents a full set of claims showing markups of the claims with insertions and deletions indicated by underlining (or double bracketing) and strikethrough text, respectively.

1. (Currently amended) An anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least one single domain antibody directed against EGFR.

2. (Currently amended) An anti-EGFR polypeptide according to claim 1 wherein the at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 1 to 22.

3. (Currently amended) An anti-EGFR polypeptide according to claim 1, ~~claims 1 and 2~~ further comprising at least one single domain antibody directed against a serum protein.

4. (Currently amended) An anti-EGFR polypeptide according to claim 1, ~~any of claims 1 to 3~~ further comprising at least one single domain antibody selected from the group consisting of anti-IFN-gamma single domain antibody, anti-TNF-alpha single domain antibody, anti-TNF-alpha receptor single domain antibody and anti-IFN-gamma receptor single domain antibody.

5. (Currently amended) An anti-EGFR polypeptide according to claim 1, ~~any of claims 1 to 4~~, wherein the number of single domain antibodies directed against EGFR is at least two.

6. (Currently amended) An anti-EGFR polypeptide according to claim 1, ~~any of claims 1 to 5~~ wherein the at least one single domain antibody is a *Camelidae* VHH.

7. (Currently amended) An anti-EGFR polypeptide according claim 1, ~~any of claims 1 to 6~~ wherein the at least one single domain antibody is a humanised *Camelidae* VHH.

8. (Currently amended) An anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 7~~, wherein said at least one single domain antibody is an homologous sequence, a

functional portion, or a functional portion of an homologous sequence of the full length single domain antibody.

9. (Currently amended) An anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 8~~, wherein the anti-EGFR polypeptide is an homologous sequence, a functional portion, or a functional portion of an homologous sequence of the full length anti-EGFR polypeptide.

10. (Currently amended) A method of identifying an agent that modulates the binding of an anti-EGFR polypeptide of claim 1 ~~any of claims 1 to 9~~ to Epidermal Growth Factor Receptor:

(a) contacting ~~a~~ an anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 5~~ with a target that is Epidermal Growth Factor Receptor, or a fragment thereof, in the presence and absence of a candidate modulator under conditions permitting binding between said polypeptide and target, and

(b) measuring the binding between the polypeptide and target of step (a), wherein a decrease in binding in the presence of said candidate modulator, relative to the binding in the absence of said candidate modulator identified said candidate modulator as an agent that modulates the binding of an anti-EGFR polypeptide of claim 1 ~~any of claims 1 to 9~~ and Epidermal Growth Factor Receptor.

11. (Currently amended) A method of identifying an agent that modulates Epidermal Growth Factor Receptor mediated disorders through the binding of an anti-EGFR polypeptide of claim 1 ~~any of claims 1 to 9~~ to Epidermal Growth Factor Receptor comprising:

(a) contacting an anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9~~ with a target that is Epidermal Growth Factor Receptor, or a fragment thereof, in the presence and absence of a candidate modulator under conditions permitting binding between said polypeptide and target, and

(b) measuring the binding between the polypeptide and target of step (a), wherein a decrease in binding in the presence of said candidate modulator, relative to the binding in the absence of said candidate modulator identified said candidate modulator as an agent that modulates Epidermal Growth Factor Receptor-mediated disorders.

12. (Currently amended) A method of identifying an agent that modulates the binding of Epidermal Growth Factor ~~Receptor~~ to its receptor through the binding of an anti-EGFR polypeptide of claim 1 ~~any of claims 1 to 9~~ to Epidermal Growth Factor Receptor comprising:

(a) contacting an anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9~~ with a target that is Epidermal Growth Factor Receptor, or a fragment thereof, or homologous sequence thereof, in the presence and absence of a candidate modulator under conditions permitting binding between said polypeptide and target, and

(b) measuring the binding between the polypeptide and target of step (a), wherein a decrease in binding in the presence of said candidate modulator, relative to the binding in the absence of said candidate modulator identified said candidate modulator as an agent that modulates the binding of Epidermal Growth Factor Receptor natural ligand.

13. (Currently amended) A kit for screening for agents that modulate Epidermal Growth Factor Receptor-mediated disorders comprising an anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9~~ and Epidermal Growth Factor Receptor, or a fragment thereof ~~thereof~~.

14.-15. (Canceled)

16. (Currently amended) The method ~~An unknown agent~~ according to claim 11 wherein said disorders are one or more of cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung.

17. (Currently amended) A nucleic acid encoding a polypeptide of claim 1 ~~any of claims 1 to 9~~.

18. (Currently amended) A method for treating and/or preventing and/or alleviating disorders relating to cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung, comprising administering to a subject in need of such treatment an effective amount of the ~~An~~ anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9 or a nucleic acid according to claim 17, or an agent according to any of claims 14 to 16 for treating and/or preventing and/or alleviating disorders relating to cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung~~.

19. (Currently amended) A method for the preparation of a medicament for treating and/or preventing and/or alleviating disorders relating to cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung, comprising combining the ~~Use of an~~ anti-EGFR polypeptide according to claim 1 and a carrier ~~any of claims 1 to 9 or a nucleic acid according to claim 17, or an agent according to any of claims 14 to 16 for the preparation of a medicament for treating and/or preventing and/or alleviating disorders relating to cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung~~.

20. (Currently amended) A method for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist that passes through the gastric environment without being inactivated, comprising administering to a subject in need of such treatment an effective amount of the ~~An~~ anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9 for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist that is able pass through the gastric environment without being inactivated~~.

21. (Currently amended) A method for the preparation of a medicament for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist that passes through the gastric environment without being inactivated, comprising combining the ~~Use of~~ anti-EGFR polypeptide according to claim 1 and a carrier ~~claims 1 to 9 for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist that is able to pass through the gastric environment without being inactivated~~.

22. (Currently amended) A method for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist to the vaginal and/or rectal tract without inactivation, comprising administering to a subject in need of such treatment an effective amount of the ~~A~~ anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9 for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist to the vaginal and/or rectal tract without inactivation~~.

23. (Currently amended) A method for the preparation of a medicament for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist to the vaginal and/or rectal tract without inactivation, comprising combining the ~~Use of a~~ anti-EGFR polypeptide according to claim 1 and a carrier ~~claims 1 to 9 for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist to the vaginal and/or rectal tract without inactivation~~.

24. (Currently amended) A method for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist to the upper respiratory tract and lung without inactivation, comprising administering to a subject in need of such treatment an effective amount of the ~~A~~ anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9 for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist to the upper respiratory tract and lung without inactivation~~.

25. (Currently amended) A method for the preparation of a medicament for treating and/or preventing and/or alleviating the symptoms of disorders requiring the delivery of a therapeutic compound to the upper respiratory tract and lung, comprising combining the ~~Use of a~~ anti-EGFR polypeptide according to claim 1 and a carrier ~~claims 1 to 9 for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders requiring the delivery of a therapeutic compound to the upper respiratory tract and lung~~.

26. (Currently amended) A method for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist to the intestinal mucosa without inactivation, wherein said disorder increases the permeability of the intestinal mucosa, comprising administering to a subject in need of such treatment an effective amount of the ~~A~~ anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9 for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist to the intestinal mucosa without inactivation, wherein said disorder increases the permeability of the intestinal mucosa~~.

27. (Currently amended) A method for the preparation of a medicament for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist without inactivation, wherein said disorder increases the permeability of the intestinal mucosa, comprising combining the ~~Use of a~~ anti-EGFR polypeptide according to claim 1 and a carrier ~~claims 1 to 9 for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist without inactivation, wherein said disorder increases the permeability of the intestinal mucosa~~.

28. (Currently amended) A method for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist to the tissues beneath the tongue without inactivation, comprising administering to a subject in need of such treatment an effective amount of the ~~A~~ anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9 for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist to the tissues beneath the tongue without inactivation~~.

29. (Currently amended) A method for the preparation of a medicament for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist to the tissues beneath the tongue without inactivation, comprising combining the ~~Use of a~~ anti-EGFR polypeptide according to claim 1 and a carrier ~~any of claims 1 to 9 for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist to the tissues beneath the tongue without inactivation~~.

30. (Currently amended) A method for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist through the skin without inactivation, comprising administering to a subject in need of such treatment an effective amount of the ~~A~~ anti-EGFR polypeptide according to claim 1 ~~any of claims 1 to 9 for treating and/or preventing and/or alleviating disorders susceptible to modulation by the delivery of an EGFR antagonist through the skin without inactivation~~.

31. (Currently amended) A method for the preparation of a medicament for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by

the delivery of an EGFR antagonist through the skin without inactivation, comprising combining the ~~Use of a~~ anti-EGFR polypeptide according to claim 1 and a carrier ~~any of claims 1 to 9 for the preparation of a medicament for treating, preventing and/or alleviating the symptoms of disorders susceptible to modulation by the delivery of an EGFR antagonist through the skin without inactivation~~.

32. (Currently amended) A method ~~polypeptide, nucleic acid or agent according to claim 18, use of a polypeptide, nucleic acid or agent according to claim 19,~~ a polypeptide according to claim 20, ~~any of claims 20, 22, 24, 26, 28 and 30, use of a polypeptide according to any of claims 21, 23, 25, 27, 29 and 31~~ wherein said disorders are cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung.

33. (Currently amended) A composition comprising a polypeptide according to claim 1 ~~any of claims 1 to 9 or a nucleic acid according any of claims 17, or an agent according to any of claims 14 to 16~~, and a suitable pharmaceutical vehicle.

34. (Currently amended) A method of diagnosing a disorder characterised by the dysfunction of EGFR comprising:

(a) contacting a sample with a polypeptide according to claim 1 ~~any of claims 1 to 9~~,

(b) detecting binding of said polypeptide to said sample, and

(c) comparing the binding detected in step (b) with a standard, wherein a difference in binding relative to said sample is diagnostic of a disorder characterized by dysfunction of EGFR.

35. (Canceled)

36. (Currently amended) A kit for screening for a disorder characterised by the dysfunction of EGFR ~~cited in claim 34~~ comprising an isolated polypeptide according to claim 1 ~~any of claims 1 to 9~~.

37. (Currently amended) A method for purification of EGFR comprising contacting a sample containing EGFR with ~~Use of~~ a polypeptide according to claim 1 ~~any of claims 1 to 9 for the purification of EGFR~~.

38. (Currently amended) A method for inhibiting interaction between EGF and one or more EGFR comprising contacting a sample containing EGF and one or more EGFR with ~~Use of~~ a polypeptide of claim 1 ~~any of claims 1 to 9 for inhibiting the interaction between EGF and one or more EGFR~~.

39. (Currently amended) A method for producing a polypeptide according to claim 6 ~~any of claims 1 to 9~~ comprising the steps of:

(a) obtaining double stranded DNA encoding a *Camelidae* species single domain heavy chain antibody directed against ~~to~~ EGFR ~~or a fragment thereof~~,

(b) cloning and expressing the DNA obtained ~~selected~~ in step (a) ~~(b)~~.

40. (Currently amended) A method of producing a polypeptide according to claim 1 ~~any of claims 1 to 9~~ comprising

(a) culturing host cells comprising nucleic acids ~~acid capable of encoding~~ that encode a polypeptide according to claim 1 ~~any of claims 1 to 9~~, under conditions allowing the expression of the polypeptide, and,

(b) recovering the produced polypeptide from the culture.

41. (Currently amended) A method according to claim 40, wherein said host cells are bacterial cells or yeast cells.

42. (Currently amended) A kit for screening for cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung, comprising a polypeptide according to claim 1 ~~claims 1 to 9~~.

43. (Currently amended) A therapeutic composition comprising:
(a) a VHH which inhibits the growth of human tumor cells by said VHH binding to Epidermal Growth Factor Receptor of said human tumor cells ~~tumour cell~~, and
(b) an anti-neoplastic agent.

44. (Currently amended) A therapeutic composition of claim 43 configured for separate administration of the components.

45. (Currently amended) A therapeutic composition of claim 43 ~~claims 43 and 44~~ wherein the human tumor cells are of ~~cancer is selected from the group consisting of~~ cancer of the breast, cancer of the ovary, cancer of the testis, cancer of the lung, cancer of the colon, cancer of the rectum, cancer of the pancreas, cancer of the liver, cancer of the central nervous system, cancer of the head and neck, cancer of the kidney, cancer of the bone, cancer of the blood ~~and~~ or cancer of the lymphatic system.